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GROUP 150

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT Application of

Helmut HETTCHE

Serial No. 07/268,772

Group Art Unit: 158

Filed: November 9, 1988

Examiner: P. Prater

For: AZELASTINE - CONTAINING MEDICAMENTS

DECLARATION UNDER 37 CFR 1.132

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Dear Sir:

I, Istvan Szelenyi, declare and state as follows:

1. I am a physician, and my training and experience have made me familiar with the effect of substances in treatment of the effects of allergins on nasal and eye tissues. Experiments have been conducted under my supervision to determine the effects of compounds disclosed in the above-identified application and the cited U.S. Patent 4,704,387.
2. The experiments are based on the fact that an allergic reaction in the eyes or the nose results from the liberation of histamine from mast cells as a result of the action of an antigen. The liberated histamine causes rhinitis symptoms.
3. The effectiveness of azelastine in preventing these symptoms in the eyes and the nose can be determined by measuring its effectiveness in preventing the liberation of histamine from sensitized rat peritoneal mast cells. The sensitivity of the cells is achieved through treatment with ovalbumin. The mast cells are incubated first with a test substance and then challenged with antigen. The amount of histamine released

is measured, and this is compared with the total potential release of histamine. The amount of inhibition of histamine release is calculated for each test substance. The test procedure is described in the attached Appendix A.

4. In the case of azelastine, the inhibition of liberation of histamine was 47.1% whereas, in the case of the compound of Example 1 of the cited Engel patent, the inhibition was only 24.4%.

5. Thus, azelastine was about twice as effective as the compound of Example 1 of the Engel patent.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

07/23/90


Istvan Szelenyi